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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
1638	11

DATE MAILED: 06/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/807,721	DANIELL ET AL.
	Examiner	Art Unit
	Anne R. Kubelik	1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-7, 11-40 and 44-50* is/are pending in the application.

4a) Of the above claim(s) *11-27,34-40 and 44-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 28-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-7 and 28-33) in Paper No. 9, filed 17 March 2003, is acknowledged. The traversal is on the ground(s) that the amendments to the claims ensure that the technical features of all group relate to a vector encoding a chaperonin and a multimeric chain immunoglobulin; thus Mayfield et al no longer discloses the technical feature. Applicant also urges that Mayfield et al failed to show enabled expression of a dimeric IgA because assembly is multimeric antibodies requires the presence of a chaperonin.

This is not found persuasive because as amended, Groups IV-VI do not have a chaperonin as a technical feature. Thus, the technical feature linking the groups is a plastid transformation vector encoding a multimeric immunoglobulin. This feature is taught by Mayfield et al (WO 98/31823). The vector itself is enabled; thus Applicant's arguments regarding enablement of methods of expression are moot.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-7 and 28-33 are examined. Claims 11-27, 34-40 and 44-50 are withdrawn from consideration as being drawn to non-elected inventions.

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Sequence identifiers are missing from pg 29, lines 1, 3 and 9-10.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules

and a response to the issues set forth below. Failure to fully comply with both of these requirements in the time period set forth in this Office action will be held to be non-responsive.

3. The specification is objected to because it has a Table 2, but no Table 1. The specification refers to Table 1 on pg 17, line 22. Correction, without introduction of new matter, is required.

4. The drawings are objected to because nothing can be made out in Figures 4A and 4B, the top portion of Figure 5, Figure 6A, and Figure 7; these figures all consist of black boxes. Corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. See 37 CFR 1.85(a) and MPEP 608.02(b).

Claim Objections

5. Claims 1-7 and 28-33 are objected to because of the following informalities:

Claims 1-6 and 28-33 are objected to because of the misspelling "mutimeric", in claim 28 more than once.

In claim 1, an article is missing before "transcription" in line 5.

In claims 2-6 a comma is missing after "1" in line 1, in claim 7 a comma is missing after "4" in line 1, and in claims 29-33 a comma is missing after "28" in line 1.

In claim 28 there should be no comma after "cell" in line 3 or after "components" in line 4.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-7 and 28-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn to plastid transformation vectors comprising plastid DNA, a plastid promoter, a selectable marker sequence, a DNA encoding a portion of an immunoglobulin, and DNA encoding an chaperonin, and transcription termination region, and additional plastid DNA sequence and methods of using the vectors to transform plastids.

The instant specification, however, only provides guidance for construction of an tobacco plastid expression vector comprising an expression cassette comprising the Guy's 13 heavy chain variable region fused to the mouse IgA2m(2) constant region followed by the Guy's 13 light chain variable region fused to the human kappa constant region (example 1A); transformation of the vector into *E. coli* and analysis of its expression (example 1B); transformation of the vector into tobacco and analysis of the expression of the RNA and protein (examples 1C-F). The specification provides general guidance for Elisa Assay for testing the effectiveness of the antibody produced in the plastids (examples (G-H), and optimization of codon usage (example 2). The specification provides prophetic expression of a construct encoding an IgA heavy chain, a light chain, a J chain and a secretory component or encoding ICAM-1 in tobacco plastids (examples 3-5).

The instant specification fails to provide guidance for plastid transformation vectors comprising plastid DNA, a plastid promoter, a selectable marker sequence, a DNA encoding a portion of an immunoglobulin, and DNA encoding an chaperonin, and transcription termination region, and additional plastid DNA sequence. The specification fails to provide guidance for plastid transformation vectors that have flanking sequences that allow the vector to be targeted to the genome of any chloroplast.

The region of the tobacco plastid genome commonly used for targeting of transformation vectors is not present in the same configuration or sequence in the genomes of other plastids. For example, rice lacks the orf131/orf70B gene (Kanno et al, 1993, Curr. Genet. 23:166-174; see Figure 3). The specification fails to teach a region of the plastid genome that is homologous across all plastid-containing organisms.

The instant specification also fails to teach transformation of the plastids of any plant species other than tobacco. Heifetz (2000, Biochimie 82:655-666) teaches that reliable and efficient plastid transformation and regeneration of fertile plants with transformed plastids has been limited to tobacco and potato (pg 658, right column, paragraph 2).

It is not clear that expression of a chaperonin and an immunoglobulin, expressed form the same vector, is possible in a plastid, as Applicant did not do this expression.

As the specification does not describe the transformation of any plant with a plastid transformation vector comprising plastid DNA, a plastid promoter, a selectable marker sequence, a DNA encoding a portion of an immunoglobulin, and DNA encoding an chaperonin, and transcription termination region, and additional plastid DNA sequence, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed

by the claims and plants or algae transformed therewith, to identify those with that express imunnoglobulin in their plastids, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, and lack of guidance in the specification as discussed above, the instant invention is not enabled.

8. Claims 1-7 and 28-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of plastid transformation vectors comprising plastid DNA, a plastid promoter, a selectable marker sequence, a DNA encoding a portion of an immunoglobulin, and DNA encoding an chaperonin, and transcription termination region, and additional plastid DNA sequence. In contrast, the specification only describes a plastid transformation vector that lacks the DNA encoding the chaperonin. Applicant does not describe any vectors encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described plastid transformation vectors comprising plastid DNA, a plastid promoter, a selectable marker sequence, a DNA encoding a portion of an immunoglobulin, and DNA encoding an chaperonin, and transcription termination region, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.
> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.
> ... the claimed genera of vertebrate and mammal cDNA are not described by the general language of the '525 patent's written description supported only by the specific nucleotide sequence of rat insulin.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-7 and 28-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claim 1 lacks antecedent basis for the limitations "the plastid DNA sequence" in lines 2-3, "the spacer sequence" in line 3, "said plastids" in line 3, "said plastid" in line 6, and "the 3' part of the plastid DNA sequence" in line 6.

Claim 1 is indefinite in its recitation of "a 5' part of the plastid DNA sequence inclusive of the spacer sequence" in lines 2-3. It is unclear what the spacer sequence is and what part of the plastid DNA is considered 5'.

Claim 1 is indefinite in its recitation of "the 3' part of the plastid DNA sequence" in line 6. It is unclear what the spacer sequence is and what part of the plastid DNA is considered 3'.

Claims 6 and 33 are indefinite in their recitation of "guised to an operative ligand". It is unclear what the ligand is operative for and what the ligand is bound by.

Claim 7 is indefinite in its recitation of "an intervening stop codon". It is unclear how an intervening stop codon differs from other stop codons.

Claim 28 lacks antecedent basis for the limitations "said cells" in line 8 and "said heterologous DNA" in lines 8-9.

Claim 28 is indefinite in its recitation of "DNA encoding immunoglobulin multimeric chain coding sequences". DNA can encode a protein but it does not encode coding sequences.

11. Claims 1-7 and 28-33 are free of the prior art, given the failure of the prior art to teach or suggest plastid transformation vectors comprising coding sequences for a chaperonin and an immunoglobulin.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
May 20, 2003